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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/881,909
Filing Date: June 15, 2001
Appellant(s): WISNIEWSKI et al.

Brett M. Hutton
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed June 14, 2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

This is one of four related appeals that the Board is urged to take up simultaneously. These three appeals applications are: SN 08/895,936, SN 10/057,610, SN 09/881,909 and SN 10/056,237.

(3) Status of Claims

The statement of the status of the claims at the time of the final office action is correctly reproduced at the bottom of page 3 of the Brief.

(4) Status of Amendments After Final

The statement of the status of the claims contained in the Brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is deficient because it does not reference any portion of the specification nor make any reference to any drawing or reference numerals.

Figures 1 and 2 constitute the elected species and are described on page 8, line 17 through page 10, line 16 of the specification, which is incorporated here by reference.

(6) Issues

The appellant's statement of the issues in the brief is substantially correct. The changes are as follows: Issue 2 is an issue that the board of Appeals have no jurisdiction over. The PTO does not decide such matters.

(7) Grouping of Claims

The appellant's statement in the brief that certain claims do not stand or fall together is not agreed with because claims 11 and 38 are identified as a first separate group, claims 23 and 54 as a second separate group and claims 29 and 55 as a third separate group. Claims 11 and 38 are separately argued on pages 23-24 of the Brief however the Examiner could find no separate arguments directed to the second group (claims 29 and 55) and the third group (claims 11 and 38).

Appellant's brief includes a statement that claims s 11 and 38 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

It is understood that appealed claims 1-10, 12-22, 24-28 and 30-53 stand or fall together based on Appellant's grouping. Appealed claims 11 and 38 stand or fall together as a separate group. As to the first group, the only independent claims are claims 1 and 30. In addition, Appellant has identified claims 23 and 54 as a separate group and claims 29 and 55 as a separate group, but has presented no separate arguments as to these latter groups.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

"Large-Scale Freezing and thawing of Biopharmaceutical Drug Product" Richard Wisniewski and Vincent Wu, (both employed at Genentech), Proceedings of the International Congress, Advanced Technologies for Manufacturing of Aseptic & Terminally Sterilized Pharmaceutical & Biopharmaceuticals, Basel, Switzerland, 17-19 February 1992, Convention Center Basel, pp 132-139.

3,550,393	Euwema	12/1970
5,535,598	Cothern et al	7/1996

"Studies of Heat Transfer From a Vertical Cylinder, With or Without Fins, embedded in a Solid Phase Change Medium," B. Kalhori and S. Ramadhyani, Transactions of the ASME, Journal of Heat Transfer, Vol. 107, February 1985, pp. 44-51.

983,466	Voorhees	2/1911
3,318,105	Burroughs et al	5/1967
2,128,572	Finnegan	9/1938
1,874,578	Morrison	8/1932
JP 57-58087	Nakao	4/1982

2,114,642	West	4/1938
2,915,292	Gross	12/1959
2,391,876	Brown	1/1946
JP 3-43390	Nagashio	2/1991
JP 6-64094	Koerber et al	3/1994

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-5, 7-10, 12-34, 36, 37 and 39-55 are rejected under 35 U.S.C. 102(b) or, in the alternative, under 35 U.S.C. 103(a). This rejection is set forth in a prior Office Action, mailed on 02/24/2004, beginning on page 14.

Claims 1-5, 7-10, 12-34, 36, 37 and 39-55 are rejected under 35 U.S.C. 103(a). This rejection is set forth in a prior Office Action, mailed on 02/24/2004, beginning on page 16.

Claims 1-5, 7-10, 12-34, 36, 37 and 39-56 [*sic* 55] are rejected under 35 U.S.C. 103(a). This rejection is set forth in a prior Office Action, mailed on 02/24/2004, at the bottom of page 22.

Claims 1-5, 7-10, 12-34, 36, 37 and 39-56 [*sic* 55] are rejected under 35 U.S.C. 103(a). This rejection is set forth in a prior Office Action, mailed on 02/24/2004, beginning on page 26.

Claims 11 and 38 are rejected under 35 U.S.C. 103(a). This rejection is set forth in a prior Office Action, mailed on 02/24/2004, beginning on page 27, top.

Claims 6 and 35 are rejected under 35 U.S.C. 103(a). This rejection is set forth in a prior Office Action, mailed on 02/24/2004, beginning on page 27, bottom.

(11) Response to Argument

I. Appellant's argument begins on page 5 of the Brief and the examiner addresses his remarks in the order presented there.

First, the Wisniewski and Wu prior art inherently forms a thermal bridge, counsel's remarks to the contrary notwithstanding. Second, there is no evidence that the remainder of the prior art relied upon by the Examiner "describe .... completely different principles [of operation] ..." None.

Appellant now appears to agree, based on his approving quotations of the Examiner spanning pages 5-6 of the Brief, that Mr. Wisniewski's first declaration cannot possibly be relied upon to be accurate given that the recognized state of the art requires

either measurement or computer modeling and the first Wisniewski declaration was not so generated, putting it, at best, into the realm of hopeful speculation.

Moreover counsel's conclusion that reference cannot be combined because the detailed temperatures distributions of the resulting structure require numerical or experimental verification is simply not comprehensible. It makes no sense. It does not follow that because accurate prediction of temperature distributions require numerical solution or experimental verification, that it would be unobvious to use bigger fins in the Wisniewski and Wu prior art, to improve heat transfer. Counsel confuses the ability to predict temperature distributions using "thought experiments" (as Mr Wisniewski purports to do in his first declaration) with the recognition, by one of ordinary skill in the art, that a heat exchanger with bigger fins transfers more heat and has either desirable attributes.

In the middle of page 6 of the Brief it states that the "First and Second Wisniewski Declaration were supported by experimentation". This is simply not true. For counsel to suggest it undermines his own credibility. See SN 08/895,936, Paper No. 33, page 12, lines 24-26 where it states clearly that they were neither experimentally nor computer generated, nor could they have been given Mr. Wisniewski's failure to recall the necessary relevant dimensions of the 1992 prior art that he, Mr. Wisniewski, and Mr. Wu developed while they were employed at Genentech.

Appellant argues that biopharmaceuticals are so different that none of the prior art relied upon by the Examiner can be relied upon (because materials other than

biopharmaceuticals are being frozen) to teach anything in regard to biopharmaceuticals. Given the number of disparate biopharmaceuticals Appellants have disclosed in the specification that can be processed in their device, the Examiner maintains all reference related to freezing of food, comestibles and juices are relevant for the reason stated in the final office action. Appellant, in an unlikely admission of pages 5-6 of the Brief, quotes the Examiner with approval, suggesting that Mr. Wisniewski's Exhibits B-D of the first declaration are not credible. Contrary to the sentence in the middle of page 6 of the Brief, Exhibits B-D were not the product of experimental or computer computation. They were by their own terms Mr. Wisniewski's: "best of my knowledge" and "reasonably resembles" guesses. There is no evidence they were experimental or generated with a computer (see Paper No. 33, page 12, lines 24-26) of SN 08/895,936. And how could they be, when Mr. Wisniewski, has been unable to remember the dimensions of the prior art device? How could be generate computer results if he couldn't even remember how big the prior art device was? In SN 08/895,936 Paper No. 33, page 12 lines 24-26, where Appellant admits they are neither experimental nor computer generated.

Beginning on page 7 of the Brief Appellant argues that there is no downward gradient of temperature between the distal end of the fin and the wall of the container in the Wisniewski and Wu prior art. On pages 3-13 of the final rejection the examiner proved this to be incorrect because of Mr. Wisniewski incorrectly assuming the temperature of the central structure and tank wall were identical. They are not as was shown on page 7 of the final rejection. The central structure is, during the cooling mode

always warmer than the container wall because of the fact that the coolant flows through the wall first and then (now warmed) through the central heat exchange structure. If one waits long enough, a downward temperature slope must occur between the fin tip and container wall. This fact simply follows from Fourier's law of heat conduction as the Examiner's analysis in the final rejection shows. No amount of opining by Mr. Wisniewski can change this fact.

Essentially two things are wrong with Exhibits B-D of the first declaration of Mr. Wisniewski.

First, Mr. Wisniewski incorrectly assumes that the fluid (c) in the jacket and the heat exchanger immersed in the biopharmaceutical are at the same temperature. They are not in the 1992 Wisniewski and Wu prior art as a consequence of the coolant going through the jacket first (and absorbing heat) and then the warmed coolant (i.e. hotter coolant than the entered the jacket) is piped to the centrally located heat exchanger. There can be absolutely no doubt that, when the entire content of the tank is frozen, the downward gradient temperature must exist between the tip of the fin and the interior wall of the container because the fluid going through the heat exchanger pipe is always warmer than the fluid going through the jacket. Thus, it is beyond dispute that once the entire contents of the tank are frozen, the warmer coolant in the centrally located heat exchange structure and the cooler coolant in the jacket will cause the thermal gradient to be downward from the tip of the fin towards the jacket wall (i.e. in the thermal bridge formed in the gap between these two structures). This has been made clear on the record, and Appellant has simply ignored it. See page 7 of the final rejection.

In so far as Figure 3b of the disclosure is concerned (Brief, page 8), this simply illustrates that, if you wait long enough, a downward gradient will occur. What Figure 3b does not illustrate is what happens right after the disclosed system starts up, which is more in keeping with what Exhibit B of the first Wisniewski declaration shows (i.e. before the ice has bridged). In other words, Appellant has engaged in a type of "apples to oranges" comparison in which the purported invention performance is shown at a time when the ice has bridged significantly (Figure 3b) and before the ice has bridged significantly in the case of the prior art (as purportedly shown in the Wisniewski Exhibits B and C of the first declaration pertaining to the prior art). In so far as comparing the Exhibit D of the aforementioned declaration to Figure 3b of the specification (where ice has bridged significantly in both cases) the Examiner does not find the temperature profile sketched Mr. Wisniewski for the prior art credible. The major flaw, as pointed out above, is Mr. Wisniewski's assumption that the fluid temperature in the pipe forming the heat exchange structure in the prior art is the same as the temperature in the jacket of the prior art device. It is submitted that this is never, in fact, true, when there is active heating or cooling of the contents of the tank occurring. Because the jacket and heat exchange structure are serially connected with respect to coolant flow, the heat transferred in the jacket section will always change the temperature of the coolant flowing to the heat exchange section. In the case of cooling, the coolant in the heat exchange structure will always be warmer than the coolant in the jacket and, at some point in time, the downward gradient must form between the tip of the fin and the jacket wall as a consequence of this temperature difference. Mr. Wisniewski's Exhibits B-D

are not credible because they incorrectly assume both the temperature of the jacket and heat exchange structure to be equal. It is submitted that from erroneous assumptions follow erroneous conclusions.

If Mr. Wisniewski were to measure temperature profiles in his purportedly inventive device just after cooling was started of a room temperature batch of biopharmaceutical placed in it, it is submitted that the same type of gradient as shown in Exhibit B would exist as both the heat exchange fins and jacket walls absorbed heat quickly from the warm contents of the tank. By placing bigger fins on the heat exchange structure than were apparently used in the prior art, the inventors have merely made the downward temperature gradient shown in Figure 3b of the drawing Figures happen sooner than in the prior art of 1992 Wisniewski and Wu device. It is inevitable however that the downward temperature gradient will occur in the 1992 prior art (notwithstanding Mr. Wisniewski's first declaration, which would suggest otherwise) at some point in time. It must occur at the very least once the entire contents of the tank are frozen and in the Examiner's estimation before that time (depending on how close the fin tip is spaced from the jacket wall).

What the actual temperature profiles are in the contents of the tank between those two extremes (immediately after starting and once the contents are entirely frozen) the Examiner would not hazard to guess. The fluid phenomena and heat transfer equations are so complex it is submitted that no human being, including Mr. Wisniewski, could accurately model these profiles without either empirical data (i.e. test results) or high power computers. The Board does not have to accept the Examiner's

conclusion at face value. The evidence is in the record – see the second paragraph of the Kalhori and Ramadhyani article, where they state the problem is so challenging as to be "amenable only to a numerical solution" (i.e. by computer). The Examiner is therefore very suspicious of the validity of Exhibits B-D of Mr. Wisniewski's first declaration given that no numerical techniques or experiments were used in their preparation. In effect, they amount to Mr. Wisniewski's guesses put in declaration form. Given the state of the art requiring numerical solutions, the Examiner can give Mr. Wisniewski's Exhibits B-D little weight except as guesses but in no way definitive. Compounding the lack of experimental or numerical analysis, the boundary conditions (temperature of the jacket and heat transfer structure being the same) are clearly erroneous.

I. 102(b)/103(a) over 1992 Wisniewski and Wu article

Regarding the 35 U.S.C. 102(b) aspect that Examiner maintains, for the reasons already articulated above, under the heading "Thermal Bridge", that the downward temperature gradient must occur in the prior art at some time after cooling is started and it must occur once the entire contents of the tank are frozen.

In the paragraph spanning pages 14-15 of the Brief, Appellants appear to agree with the Examiner's drawings on page 7 of the final rejection. It is noted however that Appellant's have not commented upon page 7 of the final rejection where the examiner's analysis shows a "linear temperature drop through the ice" (i.e. Appellant's downward gradient). Implicitly it is believed that Appellant's have conceded the truth of the matter asserted by failing to show any flaw in the Examiner's analysis.

Regarding the 35 U.S.C. 103(a) aspect, the Examiner maintains his reasons to increase the size of the fins into closer proximity to a jacket in the 1992 Wisniewski and Wu prior art are sound as stated to advantageously increase the rate of heat transfer (not commented upon by Appellant) and to improve the division of the tank into compartments (as indicated to be desirable in the 1992 Wisniewski and Wu prior art). Surely counsel is not arguing bigger fins would not form more distinct compartments, is he?

2. 103(a) 1992 Wisniewski and Wu article and 1986 Kalhori and Ramadhyani article

Paraffin in an excellent substance to do heat transfer experiments on because of its well understood physical properties. The fact that it demonstrates how effective large fins (extending all the way to the tank periphery) are in improving heat transfer gets lost in counsel's analysis. It clearly shows that very large fins work extremely well as is recognized by Appellant on page 13, lines 17-19 of the specification. Again, the 1986 Kalhori and Ramadhyani article is explicitly mentioned as a reference relied upon in the 1992 Wisniewski and Wu article. It is not an irrelevant reference as counsel suggests because of its failure to mention biopharmaceuticals by name. It was clearly relevant enough to include in the Appendix to the 1992 prior art (and when it was re-published in 1996) and it remains relevant here, notwithstanding counsel's eleventh hour attempt to eliminate it from consideration.

3. 103(a) 1992 Wisniewski and Wu article alone or the 1992 Wisniewski and Wu article/1986 Kalhori and Ramadhyani article and further in view of Euwema, Cothern, West, Morrison and Nakao

All of these references individually and taken in the aggregate teach reasons for extending the fins in the 1992 Wisniewski and Wu article to a point close to the jacket wall. In support of this approach see In re Gorman 18 USPQ2d 1885 (Fed. Cir. 1991) and In re GPAC 35 USPQ2d 1116 (Fed. Cir. 1995).

Each of these references teaches extending fins mounted on a heat exchange structure to a point very close to the jacket or even in contact with the jacket of the tank, (as contemplated on page 11, lines 14-16 of Appellant's specification). Appellants attempt to assert that no "thermal bridge" will form in the 1992 Wisniewski and Wu prior art modified to have longer fins which extend to the jacket wall, or nearly so, as taught by five separate secondary references. This is not credible. Figure 3b of Appellant's specification demonstrates this will happen quickly after start-up, when the fins get large enough. All liquids freeze somewhat alike and a particularly dilute biopharmaceutical (e.g. a genetically engineered virus in aqueous carrier) will freeze like the aqueous carrier (e.g. a saline or water).

Note the 1986 Kalhori and Ramadhyani article was cited to the Examiner by Appellants. If it is irrelevant, as is now contended, because it doesn't pertain to biopharmaceuticals, than why was it cited here and referenced in (Reference 29) in the 1992 Wisniewski and Wu article and the 1996 re-print of that article? There is "no different principle" of freezing in any of these references. Freezing is freezing (i.e.

charging from liquid phase to solid phase). No one of ordinary skill would be so myopic as to ignore all prior art not specifically related to biopharmaceuticals.

West is relied upon here to reach a system remarkably close in structure to that disclosed by Appellants. Appellants, with cursory analysis, suggest that there is no downward gradient in West because at the start both the central structure and jacket will conduct heat from the liquid to be cooled. That same phenomena occurs in Appellant's purportedly inventive device just after the cooling device is started, notwithstanding Appellant's seeming inability to acknowledge or comprehend that fact.

4. 103(a) further in view of conceded prior art discussed on page 1, line 22 – page 2, line 17 of the specification.

While the Examiner had hoped a sketch would be forthcoming, years ago, none has yet been prepared by Appellant, leaving it to the Examiner to "imagine" (July 14, 2003 amendment, page 3, first full paragraph, in SN 08/895,936), what such a device might look like. If the Board believes that it would be helpful to their decision, they are invited to avail themselves of 37 CFR 1.196(d) to require its production. As for the Examiner's imagination, it is easy to "image" that this prior art looks very much like Appellant's Figure 1 of the disclosure. Nonetheless, such "imagination" amounts to no more than an invitation to speculation and the PTO strives not to decide cases based on speculative prior art. Regarding the assertion that the present invention does not contemplate "no gap" between the tip of the fin and the jacket wall, this appears to be contradicted by page 11, lines 14-16 of the specification. It is submitted in this later configuration that a "gap" could exist on either side of the fin, which is anchored to the

jacket, notwithstanding Appellant's remarks to the contrary. The Examiner has strived repeatedly to get this information into the file and to the Board and takes no responsibility for the failure to have it made of record in a way that would permit meaningful comparison.

5. Gross or Brown

Appellant again reiterates that the Examiner is correct that there is a "need for the assistance of computer assistance to determine temperature distribution," seemly oblivious to the fact that the Exhibits attached to the first declaration of Wisniewski (Exhibits B-D) were generated without experimentation or computer assistance. Moreover Appellant seems to be unable to reconcile the numerical sophistication required to predict temperature with the relatively simple observation that larger fins produce better heat transfer and better compartmentation and less cryo-concentration because of the faster cooling rates possible (all of these advantages explicitly recognized in the prior art relied upon by the examiner).

Brown and Gross are simply relied upon to show and teach a helical baffle in the tank jacket which has the effect improving heat exchange by distributing the jacket fluid all the way around the tank with no "short-circuiting" between the inlet and outlet.

6. Nagashio and Koerber

Appellant does not argue these references other than for the reasons previously stated in regard to the purported deficiencies of the previous references.

2. Rule 56

While Appellant lists Rule 56 compliance as an issue on page 4 of the Brief, there is no separate argument in a corresponding portion of the Brief. Nonetheless the Examiner states for the record that the PTO does not decide compliance or non-compliance with Rule 56. Given the relevant facts that exist regarding the 1992 prior art that are not of record, the Examiner only made reasonable suggestions to Appellant as to how to obtain the information that was lacking (i.e. dimensions of the prior art device, which are not of record). Telephoning Genentech and asking them if they could provide the dimensions does not seem onerous in any way. In the worse case scenario they could simply refuse. Counsel refuses even that *de minimus* chore. Mr. Wisniewski has, at various times, stated he knew nothing more about the Genentech device than what he stated at that time, only to state new facts about the device in a subsequent response. The Examiner never made any "requirement" for Appellant to test anything contrary to counsel's assertions. The Examiner indicate that Exhibits B-D were extremely weak given that they were not test results nor generated by computer. In Appellant's response to this (Paper No. 33, page 11, line 19 – page 12, line 14 of SN 08/895,936) there were no assertions that the results in Exhibits B-D were computer generated or actual test results. Appellant simply admitted that "these temperature profiles were created at the request of the Examiner for his understanding during a previous telephonic interview."

Appellant also clearly stated in that response (Paper No. 33, page 12, lines 24-26 of SN 08/895,936): "Therefore, Applicant's have no way in which, and are not required, to obtain actual measured results or computer generated results of the 1992 Genentech

container." Contrast this last statement with the sentence spanning page 6 of the Brief, to wit: "However contrary to the Examiner's repeated accusations that appellants have conducted "thought experiments", the explanations, schematics and temperature distributions provided by Mr. Wisniewski accompanying the First [i.e. Exhibits B-D] and Second Wisniewski Declarations were supported by experimentation (e.g. see page 12 of the Specification) ..." (emphasis supplied), is simply not true. There are real credibility problems with Exhibits B-D of the First Wisniewski declaration as well as real problems with the assumptions made about the temperature of the heat exchange structure and the jacket being identical in the 1992 Wisniewski and Wu prior art, which is from a heat transfer view point an impossibility during an ongoing heating or cooling process.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

John K. Ford
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December 28, 2004

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